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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/486,334	07/18/2000	MICHEL DROUX	PH-98/080	6869

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EXAMINER

KUBELIK, ANNE R

ART UNIT	PAPER NUMBER
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1638

DATE MAILED: 07/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/486,334	Applicant(s) DROUX ET AL.	
	Examiner Anne R. Kubelik	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 March 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 6,9-11,15-23,25,26,31-59,61,62,65,70,71,75 and 77-80 is/are pending in the application.
- 4a) Of the above claim(s) 10,11,15,16,21,22 and 31-59 is/are withdrawn from consideration.
- 5) ☐ Claim(s) 9 is/are allowed.
- 6) ☒ Claim(s) 6,17-20,23,25,26,61,62,65,70,71,75 and 77-80 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 6, 9, 10-11, 15-23, 25-26, 31-59, 61-62, 65, 70-71, 75 and 77-80 are pending.
2. Claims 10-11, 15-16, 21-22 and 31-59 remain withdrawn from consideration, as being drawn to nonelected inventions. Applicant is reminded that complete reply to a final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.
3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
4. The objection to claims 9, 18, 71, 75 and 77 because of informalities is withdrawn in light of Applicant's amendment to the claims.
5. The rejection of claims 6, 9, 17-20, 23, 25-26, 60-71 and 74-77 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention is obviated by Applicant's cancellation of claims 60, 74 and 76.

Claim Rejections - 35 USC § 112

6. Claims 6, 17-20, 23, 25-26, 61-62, 65, 70-71 and 78-80 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of increasing the production of cysteine, glutathione, methionine and sulfur derivatives in a plant by transformation with a gene encoding an Arabidopsis cysteine-insensitive SATase operably linked to some transit peptides, does not reasonably provide enablement for methods of increasing the production of cysteine, glutathione, methionine and sulfur derivatives in a plant by transformation with a gene encoding any cysteine-insensitive SATase operably linked to transit

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peptides comprising plant plastid transit peptides and N-terminal portions of mature plastid proteins. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is repeated for the reasons of record as set forth in the Office action mailed 19 December 2003, as applied to claims 6, 17-20, 23, 25-26, 60-62, 65-71, 74 and 76. Applicant's arguments filed 23 March 2004 have been fully considered but they are not persuasive.

Applicant urges that SATs had been well-characterized in bacteria and plants prior to filing, and references to cloned bacterial and plant SATs are cited in the specification at pg 6 and 9 (response pg 6).

This is not found persuasive. The references on pg 6-7 are drawn to 6 enzymes in addition to SAT, and the specification does not indicate which references describe nucleic acids encoding cysteine-insensitive SATs. The references on pg 9-10 are only drawn to cysteine-sensitive SATs, and thus do not enable cysteine-insensitive SATs. Therefore, the specification does not teach cysteine-insensitive SATs from plants other than Arabidopsis and bacteria other than E. coli.

Applicant urges that the isolation of Arabidopsis sequences by functional complementation are described in the specification and Ruffet is disclosed as a reference; Applicant urges that the method can be used to obtain SAT from plants other than Arabidopsis and bacteria other than E. coli (response pg 6-7).

This is not found persuasive because the specification must teach how to make the nucleic acids used in the method, not how to find those nucleic acids.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1016:

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Conception of generalized approach for screening DNA library that might be used to identify and clone erythropoietin gene of then-unknown constitution is not conception of "purified and isolated DNA sequence" encoding human EPA, since it is not "definite and permanent idea of the complete and operative invention."

and at pg 1027

... despite extensive statements in the specification concerning all the analogs of the EPO gene that can be made, there is little enabling disclosure of particular analogs and how to make them. Details for preparing only a few EPO analog genes are disclosed. Amgen argues that this is sufficient to support its claims; we disagree. This "disclosure" might well justify a generic claim encompassing these and similar analogs, but it represents inadequate support for Amgen's desire to claim all EPO gene analogs. There may be many other genetic sequences that code for EPO-Type products. Amgen has told how to make and use only a few of them and is therefore not entitled to claim all of them.

Applicant urges that the method was used to isolate a cysteine-sensitive SAT from watermelon; thus the specification enables nucleotide sequences encoding cysteine-insensitive SATs other than SEQ ID NO:2 and SATs from plants other than Arabidopsis and bacteria other than E. coli (response pg 7).

This is not found persuasive. The watermelon SAT is cysteine-sensitive, and thus does not enable cysteine-insensitive SATs.

Applicant urges that the specification discloses suitable transit peptides at pg 13-15, and numerous ones were known in the art at the time of filing (response pg 7).

This is not found persuasive because the specification fails to teach transit peptides comprising plant plastid transit peptides and N-terminal portions of mature plastid proteins other than OTP. While transit peptides in general are broadly enabled, transit peptides comprising a plant plastid transit peptide, an N-terminal portion of a mature plastid protein linked by its N-terminus to the C-terminus of said plastid transit peptide, and a second plastid transit peptide linked by its N-terminus to the C-terminus of said N-terminal portion of a mature plastid protein are not broadly enabled; the only such transit peptide taught in the specification is OTP..

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7. Claims 6, 17-20, 23, 25-26, 61-62, 65, 70-71 and 78-80 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 19 December 2003, as applied to claims 6, 17-20, 23, 25-26, 60-62, 6571, 74 and 76. Applicant's arguments filed 23 March 2004 have been fully considered but they are not persuasive.

Applicant urges that they have provided sufficient written description for one of skill in the art to practice the claimed invention (response pg 8).

This is not found persuasive because the claims are drawn to use of cysteine-insensitive SATs from any plant or bacteria; the specification, however, only describes cysteine-insensitive SATs from *Arabidopsis* and *E. coli*. Thus, the specification does not provide written description of the invention within the full-scope of the claims.

Applicant urges that it is not necessary for the practice of the invention for the specification to set out other DNA molecules encompassed by the claims (response pg 8).

This is not found persuasive because the claims are drawn to use of cysteine-insensitive SATs from any plant or bacteria; thus, the specification must describe cysteine-insensitive SATs from a representative number of plants and bacteria. A single plant and a single bacteria do not represent the thousands and thousands of different bacteria and plants. Thus, the specification does not provide written description of the invention within the full-scope of the claims.

See *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997) at pg 1406:

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... A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.

See *University of Rochester v. G.D. Searle & Co.*, 69 USPQ2d 1886 (CA FC 2004) at page 1894:

Rochester also attempts to distinguish Fiers, Lilly, and Enzo by suggesting that the holdings in those cases were limited to composition of matter claims, whereas the '850 patent is directed to a method. We agree with the district court that that is "a semantic distinction without a difference." *Univ. of Rochester*, 249 F. Supp. 2d at 228. Regardless whether a compound is claimed per se or a method is claimed that entails the use of the compound, the inventor cannot lay claim to that subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds, or infringing methods from non-infringing methods. As the district court observed, "[t]he claimed method depends upon finding a compound that selectively inhibits PGHS-2 activity. Without such a compound, it is impossible to practice the claimed method of treatment."

Applicant urges that SAT is a well-characterized enzyme and the specification at pg 9-10 discloses that the SAT can be a cysteine-insensitive SAT such as SAT3; one of skill in the art can substitute other cysteine-insensitive SATs for the ones disclosed in the invention by referring to scientific literature and databases (response pg 8).

This is not found persuasive because cysteine-insensitive SATs from plants other than *Arabidopsis* and bacteria other than *E. coli* were not known at the time of filing.

Applicant urges that it is not necessary for the practice of the invention for the specification to set out other DNA molecules encoding transit peptides encompassed by the claims and that numerous transit peptides were known at the time of filing (response pg 8).

This is not found persuasive because the claims are broadly drawn to use of any transit peptide comprising the N-terminal portion of any mature plastid protein linked by its N-terminus to the C-terminus of any plastid transit peptide, and any second plastid transit peptide linked by its N-terminus to the C-terminus of said N-terminal portion of a mature plastid protein; the specification only describes one such transit peptide, OTP. Thus, the specification does not provide written description of the invention within the full-scope of the claims.

Claim Rejections - 35 USC § 103

8. Claims 75, 77 and 79-80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saito et al (1994, Plant Physiol. 106:887-895) in view of each of Noji et al (1998, J. Biol. Chem. 273:32739-32745) and Ruffet et al (1995, Eur. J. Biochem 227:500-509).

The claims are drawn to a method of increasing the production of cysteine and other sulfur-containing compounds in a plant or plant cells by culturing plant cells transforming with a nucleic acid encoding a cysteine-insensitive SATase in the plant cells.

Saito et al disclose tobacco plants transformed with a construct encoding the spinach cytoplasmic cysteine synthase gene alone or fused to a Rubisco *ssu* transit peptide sequence (pg 889, right column, paragraph 3-5). The transit peptide-cysteine synthase constructs had an additional two amino acids between the transit peptide and the N-terminal portion of the cysteine synthase gene; these peptides would be the same as those from a mature N-terminal portion of a protein that is located in the plastids or would be the same as a second transit peptide. These constructs were properly transported to the chloroplast and correctly processed (pg 890, right column, paragraph 2). The resulting plants showed increased production of cysteine and resistance to sulfite (pg 891, left column, paragraph 2, to pg 892, left column paragraph 2, and Figure 6). Saito et al do not disclose plants transformed with a construct encoding SATase.

Noji et al teach genes encoding cytoplasmic, chloroplastic and mitochondrial SATase genes from *Arabidopsis*, their cysteine sensitivities, and the overexpression of the genes in *E. coli* (pg 32742). The mitochondrial and chloroplastic forms would be fused to the native mitochondrial and chloroplastic transit peptides.

Ruffet et al teach a nucleic acid encoding a cytoplasmic SAT from *Arabidopsis*, wherein the SAT has a sequence of SEQ ID NO:2 (Figure 3, and pg 508, left column, paragraph 3).

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At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of increasing the production of cysteine in a plant by overexpressing a cytoplasmic cysteine synthase in a plant as taught by Saito et al, and to use a nucleic acid encoding another enzyme required for cysteine biosynthesis, SATase, as described in each of Noji et al and Ruffet et al. One of ordinary skill in the art would have been motivated to do so because of the role SATase has in regulation of cysteine biosynthesis Noji et al, pg 32744, left column, paragraph 4) and because Saito et al suggest expressing SATase in the plants for maximal cysteine formation (pg 893, left column, paragraph 1).

9. Claims 6, 9, 17-20, 23, 25-26, 61-62, 65, 70-71 and 78 are free of the prior art, given the failure of the prior art to teach or suggest a method of increasing the production of cysteine and other sulfur-containing compounds in a plant or plant cells, wherein the method consists of transforming a plant with a construct encoding a cysteine-insensitive SATase.

10. Claim 9 is allowable.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Anne R. Kubelik, Ph.D.
June 24, 2004



**ANNE KUBELIK
PATENT EXAMINER**